REMARKS

Claims 3 and 5-15 are pending. All of the pending claims are rejected. The Examiner withdraws the previous rejection under 35 USC 112, first paragraph in response to Applicants' last Amendment. As a preliminary matter, Applicants resubmit a computer disk version of the sequence listing saved in ASCII text.

Objection to the claims

The Examiner objects to claim 5 as not further limiting the independent claim 3. Applicants incorporate the recitations of claim 3 into claim 5 so that claim 5 is no longer dependent thereby obviating the objection.

The Examiner objects to claim 8 on the basis of "weight or mass." Applicants herein change the claims to read "a" weight or "a" mass thereby overcoming the rejection.

The Examiner objects to claim 15 because the Sup35 (protein) and SUP35 (gene) are used opposite to what is intended. Applicants herein change the "Sup" and "SUP" to use them according to what is intended and standard, i.e. "SUP" denotes the gene.

Rejection under 35 USC 112, second paragraph

The Examiner rejects claim 6, 8, 14 and 15 as allegedly unclear for the following reasons:

1. In claim 6, "abnormal" and "partly" are unclear;
2. In claim 8, "FTIR" is unclear and should be replaced with words not abbreviations; and
3. In claim 15, "the first 759 bp region of Sup35", "the first 639 nucleotides of Sup35" are unclear as it is not clear from where the sequence begins. Also, "the first 114 amino acids of Sup35p is incorrect if understood in view of the prior art, King *et al. PNAS* (1997) cited on the IDS.

Applicants herein delete "abnormal" and "partly" and define "FTIR." Applicants amend claim 15 to specify that the point from which the genomic or cDNA sequence is counted is from

the A of the initiation codon. Further, Applicants amend claim 15 to recite "amino acids 2-114" in place of "first 114 amino acids of sup35."

Rejection under 35 USC 112, first paragraph

The Examiner rejects claims 3, 5, and 7-15 as not enabled by the specification saying that the specification only enables a prion form of Ure2p, not normal or naturally-occurring Ure2p. The Examiner cites Wickner (1994) and Taylor *et al.* (1999) for the propositions that normal Ure2p must be converted into the abnormal prion form Ure2p and that the normal form would be soluble and would not form filaments and aggregates.

Applicants respectfully traverse. The instant specification provides sufficient teachings so that one of ordinary skill in the art knows the conditions for making a naturally occurring protein in amyloid form. The specification teaches filament induction at page 10, lines 5-12. Furthermore, these conditions are well known and documented in the art. Hence, the conditions are well known to one of ordinary skill in the art.

Rejection under 35 USC 103

A. The Examiner rejects claims 3 and 5-15 as allegedly unpatentable over Safar *et al.*, *Protein Science*, 1993, 2:2206-2216 in view of Coustou *et al.*, *PNAS* (1997), Glover *et al.*, *Cell* (1997) or Wickner, *Science* (1994). The Examiner admits that Safar *et al.* do not teach using Sup35p, Ure2p or Het-s protein. However, the Examiner relies upon each of Coustou *et al.*, *PNAS* (1997), Glover *et al.*, *Cell* (1997) or Wickner, *Science* (1994) for teaching one individually. The Examiner adds that one of ordinary skill in the art would have recognized that yeast prion analogs have the same property as mammalian prion proteins, and thus would be suitable to replace the mammalian prion proteins as an indicator. The Examiner further admits that the references, even in combination, do not teach the amount of indicator being 0.1 ng to 100 g, the Examiner says that the amount used by Safar *et al.* may be easily calculated as 140 □g.

Applicants amend claims 3 and 5 to specify that the level of degradation of the indicator is indicative of the efficiency of the sterilization process. The goal of Safar *et al.* was to study the thermal stability and conformational transitions of *scrapie* amyloid protein and its correlation

with infectivity. Safar *et al.* submitted *scrapie* amyloid protein to heat treatment and to chemical *scrapie* inactivators such as FA, SDS, additional alpha helix inducing fluorinated alcohols and TFA to measure their effect on the conformation of PrP27-30 and the ability to propagate, replicate and cause disease.

The presently claimed invention is a method for evaluating the efficiency of a sterilization process. Claims 3 and 5 have now been amended to clarify the relation between determining the level of degradation of the indicator with evaluating the efficiency of the sterilization process. Since some sterilization processes allow a significant degradation of prion proteins whereas other methods produce a weaker degradation, the methods of the present invention allow evaluating the efficacy of different sterilization processes.

Safar *et al.*, *Protein Science*, 1993, 2:2206-2216 in view of Coustou *et al.*, *PNAS* (1997), Glover *et al.*, *Cell* (1997) or Wickner, *Science* (1994)do not teach or suggest the methods presently claimed. Safar *et al.* merely teach that heat or chemical treatment can have an effect on the degradation of a prion protein and that the level of degradation can be measured by Western blot analysis. Safar *et al.* do not teach or suggest a method of evaluating the efficiency of a sterilization process using proteins described by Coustou *et al.*, Glover *et al.* or Wickner *et al.*

B. The Examiner rejects claim 9 as allegedly unpatentable over Safar *et al.*, *Protein Science*, 1993, 2:2206-2216 in view of Coustou *et al.*, *PNAS* (1997), Glover *et al.*, *Cell* (1997) or Wickner, *Science* (1994) and further in view of Feldman *et al.*, "Compatibility of medical devices and material with low-temperature hydrogen perioxide gas plasma," (1997). The Examiner admits that the primary and secondary references do not teach using low temperature gas plasma or oxidizing sterilizing agents. However, allegedly Feldman *et al.* teach using a sterilization process to inactivate a prion using oxidizing agents such as hydrogen peroxide as a form of low-temperature gas plasma (citing Column 30, line 33 through Column 34, line 42). Therefore, the Examiner says that it would have been obvious to substitute the sterilization technique of Feldman *et al.* for that used by the primary and secondary references, and the motivation to do so comes from the potential damage and safety concerns of the sterilization techniques of the primary and secondary references.

Applicants submit that the method of claim 9 is patentable since Safar *et al.* merely teach

that heat or chemical treatment can have an effect on the degradation of a prion protein and that the level of degradation can be measured by Western blot analysis. Neither Safar *et al.* nor any of the secondary references teach or suggest a method of evaluating the efficiency of a sterilization process using the proteins described by Coustou *et al.*, Glover *et al.* or Wickner *et al.*

C. The Examiner rejects claims 9, 10 and 13 as allegedly unpatentable over Safar *et al.*, *Protein Science*, 1993, 2:2206-2216 in view of Coustou *et al.*, *PNAS* (1997), Glover *et al.*, *Cell* (1997) or Wickner, *Science* (1994) and further in view of Dresdner *et al.*, U.S. Patent 5,357,636. The Examiner admits that the primary and secondary references do not teach ozone-based exposure or sodium hydroxide as chemical exposure. However, the Examiner says that Dresdner *et al.* teach ozone-based exposure or sodium hydroxide as an antiseptic composition and that one of ordinary skill in the art would recognize this as an equivalent sterilization technique to the sterilization techniques of the primary and secondary references. The Examiner further admits that the primary and secondary references do not teach a porous, permeable, or semi-permeable container. However, the Examiner says that Dresdner *et al.* teach a porous and liquid-permeable medical glove for sterilization. The Examiner adds that it would have been obvious to replace a glass container of the primary and secondary references with a porous medical glove, and that the motivation to make the modification comes from the fact that prions occur in various materials and various materials should be sterilized. Moreover, there is a reasonable expectation of success because various materials are indeed routinely sterilized.

Applicants reiterate that Safar *et al.* merely teach that heat or chemical treatment can have an effect on the degradation of a prion protein and that the level of degradation can be measured by Western blot analysis. Neither Safar *et al.* nor any of the secondary references teach or suggest a method of evaluating the efficiency of a sterilization process using the proteins described by Coustou *et al.*, Glover *et al.* or Wickner *et al.* Hence, the replacement of the glass container of Safar *et al.* with the medical glove of Dresdner does not render claims 9, 10 and 13 unpatentable.

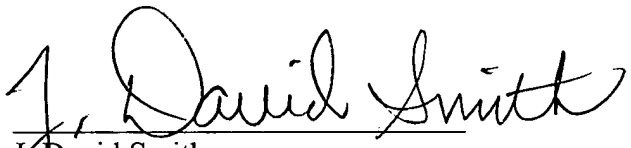
FEES

No fees are believed to be necessary. However, if any additional fees are due, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file of the instant Application. Early and favorable action on the claims is earnestly solicited. If any issues may be resolved by telephone, the Examiner is invited to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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